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TENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

| | |
|--|--|
| Date of mailing (day/month/year) 16 October 2001 (16.10.01) | |
| International application No. PCT/US01/06016 | Applicant's or agent's file reference 1486 |
| International filing date (day/month/year) 23 February 2001 (23.02.01) | Priority date (day/month/year) 23 February 2000 (23.02.00) |
| Applicant HAYEK, Carleton, S. et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
02 July 2001 (02.07.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Odile ALIU

Telephone No.: (41-22) 338.83.38

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|--|
| Applicant's or agent's file reference 1486 | <div style="display: flex; justify-content: space-between;"> <div style="text-align: center;"> FOR FURTHER ACTION </div> <div style="font-size: small;"> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. </div> </div> | |
| International application No. PCT/US 01/ 06016 | International filing date (day/month/year) 13/02/2001 | (Earliest) Priority Date (day/month/year) 23/02/2000 |
| Applicant THE JOHN HOPKINS UNIVERSITY | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

5

☐ None of the figures.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 01/06016

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Line 10: delete from "Also included..." until Line 22: "...method above."

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|--|
| Applicant's or agent's file reference 1486 | FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | |
| International application No. PCT/US 01/ 06016 | International filing date (day/month/year) 13/02/2001 | (Earliest) Priority Date (day/month/year) 23/02/2000 |
| Applicant THE JOHN HOPKINS UNIVERSITY | | |

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This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☐ the text is approved as submitted by the applicant.
- ☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- ☒ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.

5☐ None of the figures.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 01/06016

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Line 10: delete from "Also included..." until Line 22: "...method above."

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B7/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|---------------------------------------|
| Y A | WO 98 20792 A (UNIV TECHNOLOGY CORP) 22 May 1998 (1998-05-22) page 1, line 4 -page 3, line 3 page 3, line 18 - line 31 page 4, line 22 -page 7, line 8; tables 1-7 --- | 1, 2, 19, 22 3-12, 18, 20-24 |
| Y A | US 5 218 969 A (BREDESEN MARK S ET AL) 15 June 1993 (1993-06-15) abstract column 3, line 37 -column 4, line 43 column 11, line 16 -column 14, line 27; tables 2,5 --- -/-- | 1, 2, 19, 22 17, 18 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

18 July 2001

Date of mailing of the international search report

24/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040. Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Weihs, J

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| A | US 5 025 809 A (JOHNSON KEITH H ET AL) 25 June 1991 (1991-06-25) column 3, line 51 -column 4, line 65; tables 1-4 ----- | 1-5, 19, 24 |

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| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|---|--|
| WO 9820792 A | 22-05-1998 | US 5957866 A AU 5447998 A | 28-09-1999 03-06-1998 |
| US 5218969 A | 15-06-1993 | US 5010889 A WO 9409702 A AU 3126893 A US 5213108 A EP 0397787 A JP 3503962 T MX 170752 B WO 8906932 A | 30-04-1991 11-05-1994 24-05-1994 25-05-1993 22-11-1990 05-09-1991 13-09-1993 10-08-1989 |
| US 5025809 A | 25-06-1991 | NONE | |

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WO 01/62152 A1



(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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PATENT COOPERATION TREATY

PCT

REC'D 04 JUN 2002

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | |
|--|---|--|
| Applicant's or agent's file reference 1486-ARMY | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US01/06016 | International filing date (day/month/year) 13/02/2001 | Priority date (day/month/year) 23/02/2000 |
| International Patent Classification (IPC) or national classification and IPC A61B7/04 | | |
| Applicant THE JOHNS HOPKINS UNIVERSITY | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.


☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

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| Date of submission of the demand 02/07/2001 | Date of completion of this report 31.05.2002 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized officer KÖRBER, C. Telephone No. +49 89 2399 2278 |



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US01/06016

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-10 as originally filed

Claims, No.:

5-14 as originally filed

1-4,15-21 with telefax of 01/04/2002

Drawings, sheets:

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US01/06016

- ☐ the description, pages:
☒ the claims, Nos.: 22-24
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 1-18,20,21.

because:

- ☒ the said international application, or the said claims Nos. 1-18,20,21 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US01/06016

1. Statement

| | | | |
|-------------------------------|------|--------|----|
| Novelty (N) | Yes: | Claims | 19 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | 19 |
| | No: | Claims | |
| Industrial applicability (IA) | Yes: | Claims | 19 |
| | No: | Claims | |

2. Citations and explanations see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-18, 20 and 21 relate to subject-matter mentioned in Rule 67.1 (iv) PCT, in particular to diagnostic methods (even though the term "diagnosing" has been removed from claims 1 and 2, the claimed methods are implicitly diagnostic). Under terms of Art. 34(4)(a)(i) an International Preliminary Examining Authority is not required to carry out an examination of such claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents cited in the ISR:

D1: WO 98 20792 A

D2: US 5 218 969 A.

Document D1 as closest prior art discloses a method of optimizing a heart auscultation screening algorithm, comprising the following steps of claim 19: applying a heart auscultation screening time-frequency transform algorithm (102) to a set of data, wherein: said algorithm includes wavelets and bandpass filters (p. 5, l. 13); said data includes heart sounds known to be normal and heart sounds known to be pathologic (Fig. 8); said heart sounds being characterized by a systolic interval (206). The subject-matter of claim 19 differs from this known method in the systolic interval being divided into systolic sub-intervals, recording the results of said heart auscultation screening algorithm for a variety of time-frequency transform parameters and systolic sub-intervals; and determining an optimal combination of wavelet scale parameter and systolic sub-interval for use with said heart auscultation screening wavelet algorithm based on sensitivity and specificity measurements. The determination of this optimal combination allows to optimize the algorithm using known data to permit a better analysis of later acquired data (cf. section [0029] of the description of the present application). Neither D1 nor D2 disclose or suggest an optimization of the algorithm by

determining such an optimal combination. The other document cited in the IS is more remote. Consequently, the subject-matter of claim 19 meets the requirements of Article 33(2)-(4) PCT.

Further points to note:

1. The applicant should have ensured that it is explicitly clear from the description which features of the subject-matter of the independent claims are known from the prior art (see the PCT Guidelines III-2.3a).
2. The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).
3. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 and D2 is not mentioned in the description, nor are these documents identified therein.
4. The description is not in conformity with the claims as required by Rule 5.1(a)(iii) PCT.
5. The vague and imprecise statements in the description (end of sections [0017] and [0027], p. 6, l. 2, and section [0040]) imply that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

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SUBSTITUTE SHEET

PCT/US01/06016

CLAIMS:

- 1 1. A method of analyzing heart sounds comprising:
2 identifying a systolic sub-interval of a systolic interval for a plurality of heart
3 cycles in a sequence of heart cycles;
4 computing an energy value for each systolic sub-interval;
5 computing a composite energy value using the computed energy values for each
6 systolic sub-interval; and
7 comparing the composite energy value to a threshold level in order to distinguish
8 between a normal heart and a pathologic heart.
- 1 2. A method of analyzing heart sounds comprising:
2 filtering a time series of heart sounds;
3 parsing the time series of heart sounds into a sequence of individual heart cycles;
4 identifying a systolic interval for each heart cycle;
5 identifying a systolic sub-interval of the systolic interval for each heart cycle;
6 computing an energy value for the systolic sub-interval of one or more heart
7 cycles, said energy value being proportional to the energy level associated with the filtered
8 series of heart sounds;
9 computing a composite energy value for the systolic sub-intervals of one or more
10 heart cycles; and
11 comparing the composite energy value to a threshold level in order to distinguish
12 between a normal heart and a pathologic heart.
- 1 3. The method of claim 2 wherein said parsing step uses electro-cardiogram (ECG)
2 data in order to transform a time series of heart sounds into a sequence of individual heart
3 cycles.
- 1 4. The method of claim 2 wherein said parsing step uses acoustic heart sounds
2 obtained directly from a patient in order to transform a time series of heart sounds into a
3 sequence of individual heart cycles.

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SUBSTITUTE SHEET

PCT/US01/06016

1 15. The method of claim 2 wherein the composite energy value is computed as the
2 median across more than one of the heart cycle systolic sub-intervals of a quantity
3 proportional to energy.

1 16. The method of claim 2 wherein the composite energy value is computed as the
2 weighted average energy value across more than one of the heart cycle systolic sub-
3 intervals.

1 17. The method of claim 14 wherein the ratio of energies between systolic interval and
2 diastolic interval are also used to distinguish a normal heart from a pathologic heart by
3 prior statistical characterization of the ratio of energies between systolic interval and
4 diastolic interval for normal and pathologic hearts.

1 18. The method of claim 14 wherein the standard deviation of the energy in a systolic
2 interval is also used to distinguish a normal heart from a pathologic heart by prior
3 statistical characterization of the standard deviation of the energy in a systolic interval for
4 normal and pathologic hearts.

WO 01/62152

SUBSTITUTE SHEET

PCT/US01/06016

- 1 19. A method of optimizing a heart auscultation screening algorithm comprising:
2 applying a heart auscultation screening time-frequency transform algorithm to a set
3 of data, wherein:
4 said algorithm includes wavelets and bandpass filters;
5 said data includes heart sounds known to be normal and heart sounds known to
6 be pathologic;
7 said heart sounds being characterized by a systolic interval;
8 said systolic interval capable of being divided into systolic sub-intervals,
9 recording the results of said heart auscultation screening algorithm for a variety of
10 time-frequency transform parameters and systolic sub-intervals; and
11 determining an optimal combination of wavelet scale parameter and systolic sub-
12 interval for use with said heart auscultation screening wavelet algorithm based on
13 sensitivity and specificity measurements.

- 1 20. The method of claim 1 wherein the steps recite therein are contained on a computer
2 readable medium for causing a computer based system to analyze heart sounds.

- 1 21. The method of claim 2 wherein the steps recite therein are contained on a computer
2 readable medium for causing a computer based system to analyze heart sounds.

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